

## REMARKS

### Provisional Obviousness-type Double Patenting Rejection:

The Examiner has maintained the provisional obviousness-type double patenting rejection of Claims 1-38 over copending Application Serial No. 09/250,370 in view of Li et al. taken with Lucas et al. The Examiner contends that the claims of the instant application and copending Application Serial No. 09/250,370 are directed to products for cartilage repair and that, although the claims are not identical, the claimed products are not limited to the recited components. Therefore, the Examiner contends that it would have been obvious to optimize the various components and amounts thereof to provide the claimed cartilage lesion repair product in the two applications.

Applicants traverse the Examiner's provisional rejection of Claims 1-38 under the judicially created doctrine of obviousness-type double patenting. As the Examiner appears to acknowledge, the claims in the instant application and the claims in copending Application Serial No. 09/250,370 differ in the recited components and the amounts of such components in the composition. Applicants submit that the claims of the present invention recite particularly high levels of TGF $\beta$  that are not claimed in Application Serial No. 09/250,370, and that would not be obvious from the disclosure in Application Serial No. 09/250,370. Specifically, the present inventors have discovered that a relatively high concentration of TGF $\beta$  in combination with the other recited components is surprisingly chondrogenic, with very little osteogenic activity observed. The high concentration of TGF $\beta$  is recited in each of the independent claims, and it is submitted that this particular teaching regarding TGF $\beta$  was not taught or suggested in copending Application Serial No. 09/250,370. Contrary to the Examiner's assertion, Applicants submit that the quantities of proteins recited in the claims are *not mere optimization*, but are based on the present inventors discovery of what proteins and what amounts of such proteins lead toward chondrogenesis and away from osteogenesis, and therefore, the discovery can not be construed to be mere optimization. The fact that other components could be included in the composition does not dilute the novel and non-obvious teaching in the present specification regarding TGF $\beta$ . Moreover, as previously submitted, neither Li et al. or Lucas et al. teach or suggest that a TGF $\beta$  protein or any specific protein will have an impact on chondrogenesis; therefore, in the absence of the knowledge in the art that TGF $\beta$  is a variable that is effective to modulate the relative amounts of cartilage and bone produced, one can not modify the

water soluble proteins of Lucas et al., or the general reference to one or more growth factors of Li et al., to arrive at the present invention.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the provisional obviousness-type double patenting rejection over Application Serial No. 09/250,370 in view of Li et al. taken with Lucas et al.

Rejection of Claims 11, 12, 21 and 40 Under 35 U.S.C. § 112, Second Paragraph:

The Examiner has rejected Claims 11, 12, 21 and 40 under 35 U.S.C. § 112, second paragraph, for the following reasons.

With regard to Claim 12, the Examiner asserts that the recitation of "Bone Protein" is indefinite. Specifically, the Examiner states that the specification refers, at page 29, to "one method for producing Bone Protein according to the present invention", which the Examiner contends does not define what Bone Protein actually is. Applicants respectfully submit that the portion of the specification noted by the Examiner, which does refer to one method by which Bone Protein can be produced, is preceded by a portion of the specification which sets forth a definition of Bone Protein. It is believed that this definition clearly defines what Bone Protein is to one of skill in the art. In the paragraph on page 27, spanning lines 7-27, the specification states: "Bone Protein, which is defined herein as a partially-purified protein mixture from bovine long bones as described in Poser and Benedict, WO 95/13767, incorporated herein by reference in its entirety." (emphasis added) Additionally, the Amendment and Response filed on September 10, 2001 amended this portion of the specification to specifically recite the portions of WO 95/13767 that describe the partial purification process. Therefore, it is submitted that the specification clearly states that Bone Protein *is defined* as a product of a particular process, which renders Claim 12 definite. It is possible that Bone Protein as defined at page 27 could be made by another process, which is suggested at page 29, but for purposes of defining what Bone Protein is, Applicants submit that this is clearly set forth at page 27.

With regard to Claims 11, 21 and 40, the Examiner contends that it is unclear what is "CDMP". Applicants have adopted the Examiner's suggestion and have amended these claims to

B

recite the full name of the compound prior to the abbreviation. Support for this amendment is found in the specification on page 9, line 22.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejection of Claims 11, 12, 21 and 40 under 35 U.S.C. § 112, second paragraph.

Applicants submit that this application is in a condition for allowance and request the Examiner's favorable consideration of the same. In the event that the Examiner has any questions or concerns regarding this response, please consider this a provisional request for an Examiner's interview and please contact the undersigned agent at 303-863-9700.

Respectfully submitted,

SHERIDAN ROSS P.C.

By: Angela K. Dallas  
Angela K. Dallas  
Registration No. 42,460  
1560 Broadway, Suite 1200  
Denver, CO 80202-5141  
(303) 863-9700

Date: March 19, 2002

B

Marked-up Version Showing Amendments

In the Claims:

Claims 11, 21 and 40 have been amended as shown below. All other pending claims are unchanged.

11. (Twice Amended) The product of Claim 1, wherein said mixture of proteins further comprises TGF $\beta$ 2, TGF $\beta$ 3, BMP-4, BMP-5, BMP-6, cartilage-derived morphogenetic protein (CDMP), FGF-I, osteocalcin, osteonectin, BSP, lysyloxidase, cathepsin L pre, albumin, transferrin, Apo A1 LP and Factor XIIIb.

21. (Once Amended) The product of Claim 3, wherein said BMP protein is selected from the group consisting of BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, BMP-8, BMP-9 and cartilage-derived morphogenetic protein (CDMP).

40. (Once Amended) The product of Claim 3, wherein said mixture of proteins comprises TGF $\beta$ 1, TGF $\beta$ 2, TGF $\beta$ 3, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, cartilage-derived morphogenetic protein (CDMP), FGF-I, osteocalcin, osteonectin, BSP, lysyloxidase, cathepsin L pre, albumin, transferrin, Apo A1 LP and Factor XIIIb.